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09/513,086 02/24/00 MANSFIELD L MSU 4.1-458

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

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HM12/0207

WOITACH, J

EXAMINER

1632

ART UNIT	PAPER NUMBER
	02/07/01

5

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/513,086	Applicant(s) MANSFIELD ET AL.	
	Examiner Joseph Woitach	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *1-3,10-12,18-22,29-44,47 and 48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-9,13-17,23-28,45,46,49 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Pleas note that the Examiner of record and art unit has changed. The Examiner of record is now **Joseph Woitach** and the group art unit is now **1632.**

Applicants amendment filed November 14, 2000, paper number 4, has been received and entered. Note claims 1-50 are currently pending since non-elected claims have not been canceled. Claims 4 and 23 have been amended.

Applicants affirm the election of Group II, claims 4-9, 13-17, 23-28, 45-46, 49 and 50, drawn to a vaccine, methods of protecting equid via said vaccine, and method of producing polypeptides without traverse. Accordingly, claims 1-3, 10-12, 18-22, 29-44, 47 and 48 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Election was made **without** traverse and affirmed in Paper No. 4. The election has been found proper and therefore made FINAL. Claims 4-9, 13-17, 23-28, 45-46, 49 and 50 are currently under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-9, 13-17, 45-46, 49 and 50 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants state that the claims are drawn to a antigen vaccine and argue that the present invention can provide protection by producing antibodies *in vivo* which interfere with the function of surface proteins of *Sarcocystis neurona* which enable the organism to enter the nervous system or CSF. See Amendment page 3; first paragraph. Applicants argue that Liang *et al.* cited in the previous office action recognizes that Sn16 may be an important in a vaccine but does not suggest the use of recombinant proteins. Further, it is argued while Liang *et al.* suggest that Sn30 does not serve as an antigen, that the instant specification supports a possible role for Sn30 because of its ability to interfere with the Sn30 surface proteins function. In addition, Applicants argue that the vaccine trials by Fort Dodge supports the premise that a vaccine to *Sarcocystis neurona* can be developed despite the production of antibodies to whole cells and Liang *et al.* represent an invitation to experiment and does not suggest that a recombinant vaccine is produced. See Amendment pages 3-4. Applicants arguments have been fully considered but not found persuasive.

Applicant's arguments against Liang *et al.* address both the enablement issue of USC112 second paragraph and the novelty of the invention with regard to USC 102, however the basis of the instant rejection is only enablement of the invention. Stedman's Medical Dictionary defines a

vaccine as essentially any preparation intended for active immunological prophylaxis. First, Applicant states that the present vaccine does not prevent the *Sarcocystis neurona* from infecting the equid (page 3; first full paragraph, first line), however the claims clearly recites the limitation of a 'vaccine for active immunization of an equid against a *Sarcocystis neurona* infection' (claim 4). Examiner agrees with Applicants arguments that antibodies to Sn30 antigen may serve as vaccine in contrast to what Liang *et al.* teach based on the *in vitro* analysis presented in the instant specification, however the ability of antisera *in vitro* to interfere with surface proteins function does not seem to be extendable to *in vivo*. First all the samples analyzed by Liang *et al.* are samples form horses with a clinical diagnosis of neurologic disorder resembling EPM (page 1834; bottom of second column). Liang *et al.* clearly show that most of the samples maintain an immune response to Sn30 and Sn16, and that antisera from these animals are able to neutralize *S. neurona* infectivity *in vitro* (page 1836; results summarized in figure 4). However, all the animals were clinically diagnosed with some form o f neurological disorder, and so one would of ordinary skill in the art would conclude that even the presence of antibodies to Sn30 and Sn16 in an animal would not prevent the spread of *S. neurona* to the nervous system or the CSF. The specification provides evidence that antibodies to Sn30 and Sn16 can stop infection *in vitro,* however there is no evidence that they would serve as a vaccine *in vivo.* Applicants admit that the present invention does not prevent infection of equid and have not provide evidence that the invention prevents the spread of *S. neurona* to the nervous system and CSF.

Applicants have isolated the polynucleotide sequences encoding *S. neurona* Sn30 and Sn16 surface coat proteins, expressed the open reading frames of the sequences to obtain recombinant proteins and obtained antisera to said antigens. Based on *in vitro* analysis of antisera, Applicants proposed the use of isolated surface antigens of *S. neurona* for use as a vaccine, however essentially all of the work required to ultimately develop therapeutic methods has been left for others. The physiological art in general is acknowledged to be unpredictable (MPEP 2164.03). In light of the teachings of both Liang *et al.* and Kisthardt *et al.* demonstrating the presence of antisera reactivity in most horses tested, and the specific teaching of Liang *et al.* that the ability of an antibody to function *in vitro* does not correlate to function *in vivo,* the instant specification has not given the necessary teaching to provide a nexus between the proposed antigens and a functional prophylactic vaccine. As discussed above and the previous office action, there has not been a successful vaccine produced for *S. neurona.* The Applicants have not described nor provided examples of how the recited vaccine differs from those previously found in the art. Therefore, while the polynucleotide sequences encoding Sn30 and Sn16 are unique in the art of record, the specification does not provide the necessary guidance to epitopes of Sn30 or Sn16 which would serve as a vaccine *in vivo*, and one of ordinary skill in the art would be left to empirical experimentation to develop a successful vaccine if at all possible. In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue

experimentation to practice the full scope of the invention as claimed. Therefore for the reasons above and of record the rejection is maintained.

Claims 23-28 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention in the full scope of the claim is withdrawn.

Applicants argue that the methods of expressing a recombinant polypeptide are well known in the art. Further, Applicants point to the instant specification which enables expression in *E. coli.* Examiner agrees with Applicants arguments, therefore the rejection is withdrawn.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-9 and 23-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically;

Claim 4 is unclear in the recitation of 'at least one epitope of a unique 16(±4) or 30(±4) recombinant antigen of *Sacocysitis neurona* and combinations thereof' because it is not clear if 'recombinant' modifies 30(±4) or 'at least one epitope of a unique16(±4)' as well. Further, it is

unclear if 'and combinations thereof' refers to combinations of the epitopes of 16(±4) or combinations of a 30(±4) recombinant antigen and at least one epitope of 16(±4). Further, because it is unclear if recombinant modifies only 30(±4) or both 16(±4) and 30(±4), a unique 16(±4) still reads on an endogenous form of the protein.

Claim 23 is unclear in the recitation of 'a DNA encoding a fusion polypeptide comprising at least one epitope of a 16(±4) kDa antigen or 30(±4) kDa antigen or combinations thereof of *Sacocystis neurona* and an additional polypeptide that facilitates isolation of the fusion polypeptide'. As discussed above for claim 4, it is unclear if 'or combinations thereof' refers to combinations of at least one epitope of a16(±4) kDa antigen or combinations of a 30(±4) kDa antigen and at least one epitope of a 16(±4) kDa antigen. Further, it is unclear how an additional polypeptide that facilitates the fusion polypeptide is related to the 30(±4) kDa antigen and the16(±4) kDa antigen since this now can read on a second DNA encoding an antibody which recognizes a 30(±4) kDa antigen and at least one epitope of a 16(±4) kDa antigen and not physically linked to the fusion protein at all. In addition, the amendment to the claim to recite at least 'one epitope of a 16(±4) kDa antigen **or** 30(±4) kDa antigen' makes it unclear if the microorganism in a culture containing a DNA encodes a fusion protein with at least one antigen of a 16(±4) or a microorganism in a culture containing a DNA encodes an antigen of a 30(±4) which would then would encompass culturing and isolating an endogenous form of the 30(±4) protein.

The remaining dependent claims are included in the rejection because they depend on an indefinite claim and do not further serve to clarify the basis of the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 4 stands rejected under 35 U.S.C. 102(b) as being anticipated by Liang *et al.*

Applicants amendment to recite a recombinant antigen has differentiated the claimed invention from the cited reference which demonstrates only endogenous antigens produced by *Sarcocystis neurona*. Applicants arguments have been fully considered but not found persuasive.

As discussed above, the amendments to the claim 4 has necessitated a new grounds of rejection under 112 first paragraph. Since the claim is unclear and a unique 16(±4) still reads on an endogenous form of the protein and Liang *et al.* teach the immunoprecipitation and isolation of 16(±4) protein the claim is still anticipated Liang *et al.* Therefore for the reasons above and of record the rejection is maintained.

Claims 23-25 are newly rejected under 35 U.S.C. 102(b) as being anticipated by Liang *et al.*

Claims 23-25 encompass a method of for producing a polypeptide comprising providing a microorganism encoding at least one epitope of a 16(±4) kDa antigen or 30(±4) kDa antigen or combinations thereof of *Sacocystis neurona* and isolation of the polypeptide. As discussed above

in the 112 first paragraph rejection, the claim as written is unclear and presently reads on the production of a 30(±4) kDa antigen. Liang *et al.* teach that the samples were isolated from infected equid, and cell and tissue culturing conditions (page 1834; Material and Methods section). Since specific culturing conditions are not recited in the claim, the *Sacocystis neurona* in equid represent a means to culture the microorganism *in vivo*, similar to the methods taught in the specification for opossum. Further, Liang *et al.* teach the isolation of the 30(±4) kDa antigen by immunoprecipitation (page 1835; first column). Thus, Liang *et al.* teach a method of isolating a 30(±4) kDa antigen encompassed by the limitations of the claimed method.

Conclusion

No claim is allowed. Claims 4-9, 13-17, 23-28, 45-46, 49 and 50 are free of the prior art of record, however the claims are subject to other rejections.

Applicants amendments have necessitated new grounds of rejection, therefore **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach, whose telephone number is (703) 305-3732. The examiner can normally be reached on Monday through Friday from 7:00 to 5:00 (Eastern time).

If attempts to reach the examine by telephone are unsuccessful, the examiner's supervisor, Karen M. Hauda, can be reached on (703) 305-6608.

An inquiry of a general nature or relating to the status of the application should be directed to Kay Pickney whose telephone number is (703) 305-3553.

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